

WHAT IS CLAIMED IS:

1           1.       A method for loading a preservative into blood platelets comprising:  
2           providing a preservative solution having a preservative, water and protein; and  
3           loading blood platelets with the preservative solution to produce preservative-  
4 loaded blood platelets, wherein said preservative solution generally has higher glass transition  
5 temperatures than glass transition temperatures for a preservative solution having the  
6 preservative, water and no protein.

1           2.       The method of Claim 1 wherein said preservative solution in said  
2 preservative-loaded blood platelets comprises a gradient of the glass transition temperature  
3 (degrees C) to a water content ( grams of water per gram of dry weight of preservative and  
4 protein) ranging from about 50 to about 900 at a water content of less than about 0.40 grams  
5 of water per gram of dry weight of preservative and protein.

1           3.       The method of Claim 1 wherein said glass transition temperature of  
2 said preservative solution in said preservative-loaded blood platelets solution increases at a  
3 water content of less than about 0.40 grams of water per gram dry weight of preservative and  
4 protein.

1           4.       The method of Claim 1 wherein said preservative solution in said  
2 preservative-loaded blood platelets comprises a greater rate of glass transition temperature  
3 per water content (weight of water per dry weight of preservative and protein) increase at a  
4 water content of less than about 0.25 grams of water per gram dry weight of preservative and  
5 protein than at a water content greater than about 0.25 grams of water per gram dry weight of  
6 preservative and protein.

1           5.       The method of Claim 1 wherein said preservative solution in said  
2 preservative-loaded blood platelets comprises a greater rate of glass transition temperature  
3 per water content (weight of water per dry weight of preservative and protein) increase at a  
4 water content of less than about 0.15 grams of water per gram dry weight of preservative and  
5 protein than at a water content of greater than about 0.15 grams of water per gram dry weight  
6 of preservative and protein.

1           6.       The method of Claim 1 wherein said preservative solution in said  
2 produced preservative-loaded blood platelets generally has said higher glass transition

3 temperatures at a water content (weight of water per dry weight of preservative and protein)  
4 of less than about 0.25 grams of water per gram dry weight of preservative and protein.

1 7. The method of Claim 1 wherein said preservative comprises an  
2 oligosaccharide.

1 8. The method of Claim 7 wherein said oligosaccharide is trehalose.

1 9. The method of Claim 1 wherein said preservative-loaded blood  
2 platelets comprise a water content ranging from about 0.02 grams of water per gram of dry  
3 weight of preservative and protein to about 0.40 grams of water per gram of dry weight of  
4 preservative and protein.

1 10. The method of Claim 1 wherein said preservative-loaded blood  
2 platelets comprise a water content ranging from about 0.15 grams of water per gram of dry  
3 weight of preservative and protein to about 0.40 grams of water per gram of dry weight of  
4 preservative and protein.

1 11. The method of Claim 1 wherein said protein is albumin.

1 12. The method of Claim 1 wherein said albumin is bovine albumin.

1 13. The method of Claim 1 wherein a gradient of the glass transition  
2 temperature (degrees C) to the water content (grams of water per gram of dry weight of  
3 preservative and protein) ranges from about 50 to about 900 at a water content of less than  
4 about 0.30 grams of water per gram of dry weight of preservative and protein.

1 14. The method of Claim 1 wherein a gradient of the glass transition  
2 temperature (degrees C) to the water content (grams of water per gram of dry weight of  
3 preservative and protein) ranges from about 50 to about 900 at a water content ranging from  
4 about 0.02 to less than about 0.40 grams of water per gram of dry weight of preservative and  
5 protein.

1 15. The method of Claim 1 wherein a gradient of the glass transition  
2 temperature (degrees C) to the water content (grams of water per gram of dry weight of  
3 preservative and protein) ranges from about 100 to about 800 at a water content ranging from  
4 about 0.15 to about 0.30 grams of water per gram of dry weight of preservative and protein.

1           16.     The method of Claim 1 wherein a gradient of the glass transition  
2 temperature (degrees C) to the water content (grams of water per gram of dry weight of  
3 preservative and protein) ranges from about 50 to about 150 at a water content ranging from  
4 about 0.20 to about 0.30 grams of water per gram of dry weight of preservative and protein.

1           17.     The method of Claim 1 wherein a gradient of the glass transition  
2 temperature (degrees C) to the water content (grams of water per gram of dry weight of  
3 preservative and protein) ranges from about 75 to about 125 at a water content ranging from  
4 about 0.20 to about 0.30 grams of water per gram of dry weight of preservative and protein.

1           18.     The method of Claim 1 wherein a gradient of the glass transition  
2 temperature (degrees C) to the water content (grams of water per gram of dry weight of  
3 preservative and protein) ranges from about 700 to about 900 at a water content ranging from  
4 about 0.15 to about 0.20 grams of water per gram of dry weight of preservative and protein.

1           19.     The method of Claim 1 wherein a gradient of the glass transition  
2 temperature ( degrees C) to the water content (grams of water per gram of dry weight of  
3 preservative and protein) ranges from about 750 to about 850 at a water content ranging from  
4 about 0.15 to about 0.20 grams of water per gram of dry weight of preservative and protein.

1           20.     The method of Claim 1 wherein said preservative solution comprises  
2 said preservative and said protein in a weight ratio ranging from about 0.25 grams to about  
3 1.75 grams of preservative per each gram of protein.

1           21.     The method of Claim 1 wherein said preservative solution comprises  
2 said preservative and said protein in an approximate 1:1 weight ratio.

1           22.     The method of Claim 1 wherein said preservative-loaded blood  
2 platelets have said higher glass transition temperatures.

1           23.     The method of Claim 9 wherein said preservative-loaded blood  
2 platelets have said higher glass transition temperatures.

1           24.     Blood platelets produced in accordance with the method of Claim 1.

1           25.     A platelet composition comprising

2 blood platelets having a preservative solution including a preservative, water,  
3 and protein, and generally having higher glass transition temperatures than glass transition  
4 temperatures for blood platelets loaded with the preservative, water, but no protein.

1 26. The composition of Claim 25 wherein said blood platelets comprise a  
2 gradient of the glass transition temperature (degrees C) to a water content ( grams of water  
3 per gram of dry weight blood platelets) ranging from about 50 to about 900 at a water content  
4 of less than about 0.40 grams of water per gram of dry weight blood platelets.

1 27. The composition of Claim 25 wherein a gradient of the glass transition  
2 temperature ( degrees C) to the water content ( grams of water per gram of dry weight of  
3 blood platelets) ranges from about 50 to about 150 at a water content ranging from about 0.20  
4 to about 0.30 grams of water per gram of dry weight of blood platelets.

1 28. The composition of Claim 25 wherein the gradient of the glass  
2 transition temperature ( degrees C) to the water content ( grams of water per gram of dry  
3 weight preservative) ranges from about 75 to about 125 at a water content ranging from about  
4 0.20 to about 0.30 grams of water per gram of dry weight preservative.

1 29. The composition of Claim 25 wherein a gradient of the glass transition  
2 temperature ( degrees C) to the water content (grams of water per gram of dry weight of  
3 blood platelets) ranges from about 700 to about 900 at a water content ranging from about  
4 0.15 to about 0.20 grams of water per gram of dry weight of blood platelets.

1 30. The composition of Claim 25 wherein a gradient of the glass transition  
2 temperature ( degrees C) to the water content (grams of water per gram of dry weight of  
3 blood platelets) ranges from about 750 to about 850 at a water content ranging from about  
4 0.15 to about 0.20 grams of water per gram of dry weight of blood platelets.

1 31. The composition of Claim 25 wherein said preservative comprises an  
2 oligosaccharide.

1 32. The composition of Claim 31 wherein said oligosaccharide is  
2 trehalose.

1 33. The composition of Claim 25 wherein said protein comprises albumin.

1           34.     A process for processing blood platelets comprising:  
2           providing a preservative solution having a preservative, water, and protein;  
3           suspending blood platelets in the preservative solution at a concentration  
4 greater than about  $10^8$  platelets per ml. of preservative solution to produce preservative-  
5 loaded blood platelets;  
6           freeze-drying the preservative-loaded blood platelets; and  
7           recovering at least 75% of the freeze-dried platelets.

1           35.     The process of Claim 34 wherein said preservative solution comprises  
2 from about 60 mM to about 240 mM of said preservative and from about 2% by weight to  
3 about 8% by weight of said protein.

1           36.     The process of Claim 34 wherein said concentration ranges from about  
2  $0.5 \times 10^9$  platelets per ml preservative solution to about  $10.0 \times 10^9$  platelets per ml  
3 preservative solution.

1           37.     The process of Claim 34 wherein said concentration ranges from about  
2  $0.5 \times 10^9$  platelets per ml preservative solution to about  $10.0 \times 10^9$  platelets per ml  
3 preservative solution, and said recovering includes recovering at least 85% by weight of the  
4 freeze-dried platelets.

1           38.     The process of Claim 34 additionally comprising storing, prior to  
2 recovering, the freeze-dried platelets.

1           39.     A process for preserving protein structure in blood platelets  
2 comprising:  
3           providing a preservative solution having a preservative, water and protein;  
4           loading blood platelets with the preservative solution to produce preservative-  
5 loaded blood platelets;  
6           dehydrating the preservative-loaded blood platelets while maintaining a  
7 residual water content in the blood platelets equal to or less than about 0.30 gram of residual  
8 water per gram of dry weight blood platelets to preserve protein structure of the blood  
9 platelets upon rehydrating after storage;  
10          storing the dehydrated preservative-loaded blood platelets; and

11 rehydrating the stored dehydrated preservative-loaded blood platelets with  
12 water vapor to preserve protein structure of the blood platelets.

1 40. The process of Claim 39 wherein said rehydrating the stored  
2 dehydrated preservative-loaded blood platelets with water vapor comprises increasing the  
3 water content of the preservative-loaded blood platelets until the preservative-loaded blood  
4 platelets have a water content equal to or less than about 0.30 grams of water per gram of dry  
5 weight blood platelets.

1 41. The process of Claim 39 additionally comprising directly hydrating  
2 with bulk water the rehydrated preservative-loaded blood platelets.

1 42. A dehydrated composition for mammalian therapy comprising:  
2 freeze-dried platelets comprising a preservative solution for preserving  
3 biological properties during freeze-drying and rehydration, wherein said preservative solution  
4 includes water, protein, and a preservative, and said platelets are rehydratable so as to have a  
5 normal response to at least one agonist.

1 43. The dehydrated composition of Claim 42 wherein said normal  
2 response to at least one agonists includes a response to thrombin in a physiological  
3 concentration commencing at thrombin concentrations ranging from about 0.1 U/ml to about  
4 1.0 U/ml, and wherein between thrombin concentrations ranging from about 0.2 U/ml to  
5 about 0.70 U/ml, percent(%) aggregation of the rehydrated platelets ranges from about 20%  
6 to about 80%.

1 44. The dehydrated composition of Claim 42 wherein said normal  
2 response to at least one agonists includes a response to ristocetin in a physiological  
3 concentration commencing at ristocetin concentrations ranging from about 1.0 mg/ml to  
4 about 10.0 mg/ml.

5  
1 45. The dehydrated composition of Claim 42 wherein said normal  
2 response to at least one agonists includes a response to ristocetin in a physiological  
3 concentration and between ristocetin concentrations ranging from about 2.0 mg/ml to about  
4 10.0 mg/ml, percent(%) aggregation of the rehydrated platelets ranges from about 10% to  
5 about 100%.

1           46.     The dehydrated composition of Claim 42 wherein said normal  
2 response to at least one agonists includes a response to ristocetin in a physiological  
3 concentration and between ristocetin concentrations ranging from about 3.5 mg/ml to about  
4 9.0 mg/ml, percent(%) aggregation of the rehydrated platelets typically ranges from about  
5 40% to about 90%.

1           47.     The dehydrated composition of Claim 42 wherein said normal  
2 response to at least one agonists includes a response to ristocetin in a physiological  
3 concentration and between ristocetin concentrations ranging from about 4.0 mg/ml to about  
4 7.0 mg/ml, percent(%) aggregation of the rehydrated platelets ranges from about 60% to  
5 about 80%.

1           48.     A process for loading a preservative into blood platelets comprising:  
2           providing a preservative solution having a preservative, water and protein;  
3           disposing platelets in the preservative solution for loading the preservative  
4 from the preservative solution into the platelets to produce preservative-loaded blood  
5 platelets wherein said preservative solution generally has higher glass transition temperatures  
6 than glass transition temperatures for a preservative solution having the preservative, water  
7 and no protein; and  
8           preventing a decrease in a loading efficiency gradient in the loading of the  
9 preservative into the platelets.

1           49.     The process of Claim 48 wherein said preservative comprises an  
2 oligosaccharide and said preventing a decrease in a loading efficiency gradient in the loading  
3 of the oligosaccharide into the platelets comprises maintaining a concentration of the  
4 oligosaccharide in the oligosaccharide solution below about 50 mM.

1           50.     The process of Claim 48 wherein said loading comprises loading by  
2 fluid phase endocytosis.

1           51.     The process of Claim 49 wherein said loading comprises loading by  
2 fluid phase endocytosis.

1           52.     The process of Claim 48 wherein said preservative comprises an  
2 oligosaccharide and said preventing a decrease in a loading efficiency gradient in the loading



3 of the oligosaccharide into the platelets comprises maintaining a positive gradient of loading  
4 efficiency to concentration of the oligosaccharide in the oligosaccharide solution.

1 53. The process of Claim 48 wherein said preservative comprises an  
2 oligosaccharide and said preventing a decrease in a loading efficiency gradient in the loading  
3 of the oligosaccharide into the platelets comprises maintaining a positive gradient of loading  
4 efficiency (%) to concentration (mM) of the oligosaccharide in the oligosaccharide solution.

1 54. The process of Claim 52 wherein said oligosaccharide is trehalose.

1 55. The process of Claim 53 wherein said oligosaccharide is trehalose.

1 56. A process for loading a preservative into blood platelets comprising:  
2 providing a preservative solution having a preservative, water and protein;  
3 disposing platelets in the preservative solution for loading the preservative  
4 from the preservative solution into the platelets to produce preservative-loaded blood  
5 platelets wherein said preservative solution generally has higher glass transition temperatures  
6 than glass transition temperatures for a preservative solution having the preservative, water  
7 and no protein; and  
8 preventing a decrease in a loading gradient in the loading of the  
9 oligosaccharide into the platelets.

1 57. The process of Claim 56 wherein said preservative comprises an  
2 oligosaccharide and said preventing a decrease in a loading gradient in the loading of the  
3 oligosaccharide into the platelets comprises maintaining a concentration of the  
4 oligosaccharide in the oligosaccharide solution below about 50 mM.

1 58. The process of Claim 56 wherein said preservative comprises an  
2 oligosaccharide and said loading comprises loading by fluid phase endocytosis.

1 59. The process of Claim 57 wherein said loading comprises loading by  
2 fluid phase endocytosis.

1 60. The process of Claim 56 wherein said preservative comprises an  
2 oligosaccharide and said preventing a decrease in a loading gradient in the loading of the  
3 oligosaccharide into the platelets comprises maintaining a positive gradient of concentration



4 of oligosaccharide loaded into the platelets to concentration of the oligosaccharide in the  
5 oligosaccharide solution.

1 61. The process of Claim 60 wherein said oligosaccharide is trehalose.

1 62. A method for preserving platelets, said method comprising  
2 providing solute-loaded platelets, and  
3 drying the platelets in an iso-osmotic freeze drying solution to produce dried  
4 solute-loaded platelets.

1 63. A method of claim 62, wherein said dried platelets are rehydrated,  
2 without prehydration.